

CLAIMS

What is claimed is:

1. A coating composition for use in delivering a medicament from the surface of a medical device positioned *in vivo*, the composition comprising a polymeric reagent formed by the polymerization of the following monomers:
 - a) about 1 to about 20 mole % of a polyether monomer,
 - b) about 5 to about 75 mole % of a carboxylic acid-containing monomer, such that the effective ratio of ether groups to carboxylic acid groups in the resultant copolymer is between about 1 to 1 and about 10 to 1,
 - c) optionally, about 0.1 to about 10 mole % of a photoderivatized monomer, and
 - d) an amount of a hydrophilic monomer suitable to bring the composition to 100%.
2. A composition according to claim 1 wherein the polyether monomer comprises an alkoxy (poly)alkyleneglycol (meth)acrylate.
3. A composition according to claim 2 wherein the alkoxy group is selected from the group consisting of methoxy, ethoxy, propoxy, and butoxy.
4. A composition according to claim 2 wherein the (poly)alkylene glycol component of the alkoxy (poly)alkyleneglycol (meth)acrylate is selected from the group consisting of (poly)propylene glycol and (poly)ethylene glycol.
5. A composition according to claim 4 wherein the (poly)alkylene glycol has a nominal weight average molecular weight ranging from about 200 g/mole to about 2000 g/mole.

6. A composition according to claim 5 wherein the polyether monomer is selected from the group consisting essentially of methoxy (poly)ethylene glycol methacrylates, (poly)ethylene glycol methacrylates, and (poly)propylene glycol methacrylates.

7. A composition according to claim 1 wherein the polyether monomer is present in an amount of between about 5 and about 15 mole %.

8. A composition according to claim 1 wherein the carboxylic acid-containing monomer is selected from carboxyl substituted ethylene compounds.

9. A composition according to claim 8 wherein the carboxyl acid-containing monomer is selected from acrylic, methacrylic, maleic, crotonic, itaconic, and citraconic acid.

10. A composition according to claim 8 wherein the concentration of the carboxylic acid-containing monomer is between about 30 to about 50 mole %.

11. A composition according to claim 10 wherein the carboxylic-acid containing monomer comprises (meth)acrylic acid.

12. A composition according to claim 9 wherein the concentration of the carboxylic acid-containing monomer is between about 30 to about 50 mole % and the carboxylic acid containing monomer comprises (meth)acrylic acid.

13. A composition according to claim 1 wherein the photoderivatized monomer is selected from the group consisting of N-[3-(4-benzoylbenzoamido)propyl]methacrylamide, 9-vinyl anthracene, and 9-anthracenylmethyl methacrylate.

14. A composition according to claim 13 wherein the photoderivatized monomer is present in an amount of between about 1 to about 7 mole %.

15. A composition according to claim 1 wherein the hydrophilic monomer comprises an alkenyl substituted amide.

16. A composition according to claim 15 wherein the hydrophilic monomer is selected from the group consisting of acrylamide, N-vinylpyrrolidone, methacrylamide, and acrylamido propanesulfonic acid (AMPS).

17. A composition according to claim 16 wherein the hydrophilic monomer is present in an amount of between about 30 and about 70 mole %.

18. A composition according to claim 1 wherein the medicament is selected from the group consisting of peptides, proteins, carbohydrates, nucleic acids, lipids, polysaccharides and combinations thereof.

19. A composition according to claim 1 wherein the medicament is selected from the group consisting of gene therapy agents selected from therapeutic nucleic acids and nucleic acids encoding therapeutic gene products, antibiotics selected from penicillin, tetracycline, chloramphenicol, minocycline, doxycycline, vancomycin, bacitracin, kanamycin, neomycin, gentamycin, erythromycin and cephalosporins and antiseptics selected from silver sulfadiazine, chlorhexidine, glutaraldehyde, peracetic acid, sodium hypochlorite, phenols, phenolic compounds, iodophor compounds, quaternary ammonium compounds, and chlorine compounds.

20. A composition according to claim 1 wherein the device is selected from the group consisting of catheters, implantable vascular access ports, blood storage bags, vascular stents, blood tubing, central venous catheters, arterial catheters, vascular grafts, intraaortic balloon pumps, heart valves, cardiovascular sutures, total artificial hearts and ventricular assist pumps, extracorporeal devices such as blood oxygenators, blood filters, hemodialysis units, hemoperfusion units, plasmapheresis units, hybrid artificial organs such as pancreas or liver and artificial lungs and filters adapted for deployment in a blood vessel in order to trap emboli.

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A crosslinked coating composition for use in delivering a medicament from the surface of a medical device positioned *in vivo*, the composition comprising a polymeric reagent in the form of a gel matrix, the polymeric reagent being formed by the polymerization of the following monomers:

- 5 a) about 1 to about 20 mole % of a polyether monomer,
- b) about 5 to about 75 mole % of a carboxylic acid-containing monomer, such that the effective ratio of ether groups to carboxylic acid groups in the resultant copolymer is between about 1 to 1 and about 10 to 1,
- c) about 0.1 to about 10 mole % of the residue of a photoderivatized monomer, and
- d) an amount of a hydrophilic monomer suitable to bring the composition to 100%.

22. A crosslinked composition according to claim 21 wherein the polyether monomer comprises an alkoxy (poly)alkyleneglycol (meth)acrylate.

23. A crosslinked composition according to claim 22 wherein the alkoxy group is selected from the group consisting of methoxy, ethoxy, propoxy, and butoxy.

15 24. A crosslinked composition according to claim 22 wherein the (poly)alkylene glycol component of the alkoxy (poly)alkyleneglycol (meth)acrylate is selected from the group consisting of (poly)propylene glycol and (poly)ethylene glycol.

20 25. A crosslinked composition according to claim 24 wherein the (poly)alkylene glycol component has a nominal weight average molecular weight ranging from about 200 g/mole to about 2000 g/mole.

26. A crosslinked composition according to claim 25 wherein the polyether monomer is selected from the group consisting essentially of methoxy (poly)ethylene glycol methacrylates, (poly)ethylene glycol methacrylates, and (poly)propylene glycol methacrylates.

27. A crosslinked composition according to claim 21 wherein the polyether monomer is present in an amount of between about 5 and about 15 mole %.

28. A crosslinked composition according to claim 21 wherein the carboxylic acid-containing monomer is selected from carboxyl substituted ethylene compounds.

29. A crosslinked composition according to claim 28 wherein the carboxylic acid-containing monomer is selected from acrylic, methacrylic, maleic, crotonic, itaconic, and citraconic acid.

30. A crosslinked composition according to claim 28 wherein the concentration of the carboxylic acid-containing monomer is between about 30 to about 50 mole %.

31. A crosslinked composition according to claim 30 wherein the carboxylic acid-containing monomer comprises (meth)acrylic acid.

32. A crosslinked composition according to claim 29 wherein the concentration of the carboxylic acid-containing monomer is between about 30 to about 50 mole % and the carboxylic acid containing monomer comprises (meth)acrylic acid.

33. A crosslinked composition according to claim 21 wherein the photoderivatized monomer is selected from the group consisting of N-[3-(4-benzoylbenzoamido)propyl]methacrylamide ("BBA-APMA"), 9-vinyl anthracene, and 9-anthracenylmethyl methacrylate.

34. A crosslinked composition according to claim 33 wherein the photoderivatized monomer is present in an amount of between about 1 to about 7 mole %.

35. A crosslinked composition according to claim 21 wherein the hydrophilic monomer comprises an alkenyl substituted amide.

36. A crosslinked composition according to claim 35 wherein the hydrophilic monomer is selected from the group consisting of acrylamide, N-vinylpyrrolidone, methacrylamide, and acrylamido propanesulfonic acid (AMPS).

37. A crosslinked composition according to claim 36 wherein the hydrophilic monomer is present in an amount of between about 30 and about 70 mole %.

38. A crosslinked composition according to claim 21 wherein the medicament is selected from the group consisting of peptides, proteins, carbohydrates, nucleic acids, lipids, polysaccharides and combinations thereof.

39. A crosslinked composition according to claim 21 wherein the medicament is selected from the group consisting of gene therapy agents selected from therapeutic nucleic acids and nucleic acids encoding therapeutic gene products, antibiotics selected from penicillin, tetracycline, chloramphenicol, minocycline, doxycycline, vancomycin, bacitracin, kanamycin, neomycin, gentamycin, erythromycin and cephalosporins and antiseptics selected from silver sulfadiazine, chlorhexidine, glutaraldehyde, peracetic acid, sodium hypochlorite, phenols, phenolic compounds, iodophor compounds, quaternary ammonium compounds, and chlorine compounds.

40. A crosslinked composition according to claim 21 wherein the device is selected from the group consisting of catheters, implantable vascular access ports, blood storage bags, vascular stents, blood tubing, central venous catheters, arterial catheters, vascular grafts, intraaortic balloon pumps, heart valves, cardiovascular sutures, total artificial hearts and ventricular assist pumps, extracorporeal devices such as blood oxygenators, blood filters, hemodialysis units, hemoperfusion units, plasmapheresis units, hybrid artificial organs such as

pancreas or liver and artificial lungs and filters adapted for deployment in a blood vessel in order to trap emboli.

41. A method of preparing a crosslinked coating composition for use in delivering a medicament from the surface of a medical device when positioned *in vivo*, the method

5 comprising the steps of:

1) providing a polymeric reagent formed by the polymerization of the following monomers:

- a) about 1 to about 20 mole % of a polyether monomer,
- b) about 5 to about 75 mole % of a carboxylic acid-containing monomer, such that the effective ratio of ether groups to carboxylic acid groups in the resultant copolymer is between about 1 to 1 and about 10 to 1,
- c) optionally, about 0.1 to about 10 mole % of a photoderivatized monomer, and
- d) an amount of a hydrophilic monomer suitable to bring the composition to 100%,

2) applying the composition as a coating to the surface of the medical device under conditions suitable to form a gel matrix by a process that includes a complexation reaction between carboxylic acid groups and ether groups, and

3) incorporating a medicament into the composition.

42. A method according to claim 41 wherein the polyether monomer comprises an alkoxy (poly)alkyleneglycol (meth)acrylate.

43. A method according to claim 42 wherein the alkoxy group is selected from the group consisting of methoxy, ethoxy, propoxy, and butoxy.

44. A method according to claim 42 wherein the (poly)alkylene glycol component of the alkoxy (poly)alkyleneglycol (meth)acrylate is selected from the group consisting of (poly)propylene glycol and (poly)ethylene glycol.

45. A method according to claim 44 wherein the (poly)alkylene glycol has a nominal weight average molecular weight ranging from about 200 g/mole to about 2000 g/mole.

46. A method according to claim 45 wherein the polyether monomer is selected from the group consisting essentially of methoxy (poly)ethylene glycol methacrylates, (poly)ethylene glycol methacrylates, and (poly)propylene glycol methacrylates.

47. A method according to claim 41 wherein the polyether monomer is present in an amount of between about 5 and about 15 mole %.

48. A method according to claim 41 wherein the carboxylic acid-containing monomer is selected from carboxyl substituted ethylene compounds.

49. A method according to claim 48 wherein the carboxyl acid-containing monomer is selected from acrylic, methacrylic, maleic, crotonic, itaconic, and citraconic acid.

50. A method according to claim 48 wherein the carboxyl acid-containing monomer is present at a concentration of about 5 to about 75 mole %, such that the effective ratio of ether groups to carboxylic acid groups in the resultant copolymer is between about 1 to 1 and about 10 to 1.

51. A method according to claim 50 wherein the concentration of the carboxylic acid-containing monomer is between about 30 to about 50 mole %.

52. A method according to claim 49 wherein the carboxylic-acid containing monomer comprises (meth)acrylic acid.

53. A method according to claim 41 wherein the photoderivatized monomer is selected from the group consisting of N-[3-(4-benzoylbenzoamido)propyl]methacrylamide, 9-vinyl anthracene, and 9-anthracenylmethyl methacrylate.

54. A method according to claim 53 wherein the photoderivatized monomer is present in an amount of between about 1 to about 7 mole %.

55. A method according to claim 41 wherein the hydrophilic monomer comprises an alkenyl substituted amide.

56. A method according to claim 55 wherein the hydrophilic monomer is selected from the group consisting of acrylamide, N-vinylpyrrolidone, methacrylamide, and acrylamido propanesulfonic acid (AMPS).

57. A method according to claim 56 wherein the hydrophilic monomer is present in an amount of between about 30 and about 70 mole %.

58. A method according to claim 41 wherein the medicament is selected from the group consisting of peptides, proteins, carbohydrates, nucleic acids, lipids, polysaccharides and combinations thereof.

59. A method according to claim 41 wherein the medicament is selected from the group consisting of gene therapy agents selected from therapeutic nucleic acids and nucleic acids encoding therapeutic gene products, antibiotics selected from penicillin, tetracycline, chloramphenicol, minocycline, doxycycline, vancomycin, bacitracin, kanamycin, neomycin, gentamycin, erythromycin and cephalosporins and antiseptics selected from silver sulfadiazine, chlorhexidine, glutaraldehyde, peracetic acid, sodium hypochlorite, phenols, phenolic compounds, iodophor compounds, quaternary ammonium compounds, and chlorine compounds.

60. A method according to claim 41 wherein the device is selected from the group consisting of catheters, implantable vascular access ports, blood storage bags, vascular stents, blood tubing, central venous catheters, arterial catheters, vascular grafts, intraaortic balloon pumps, heart valves, cardiovascular sutures, total artificial hearts and ventricular assist pumps, extracorporeal devices such as blood oxygenators, blood filters, hemodialysis units, hemoperfusion units, plasmapheresis units, hybrid artificial organs such as pancreas or liver and artificial lungs and filters adapted for deployment in a blood vessel in order to trap emboli.

61. A method according to claim 41 wherein the medicament is incorporated into the composition prior to applying the composition to the surface.

62. A method according to claim 41 wherein the medicament is incorporated into the composition after applying the composition to the surface.

63. A method according to claim 41 wherein the medicament is incorporated into the crosslinked matrix after implanting the coated device into a tissue site.

64. A method according to claim 60 wherein the medical device is prepared from polymeric, metallic, or ceramic material and combinations thereof.

65. A method according to claim 61, wherein the device provides a polymeric surface selected from the group consisting of polyurethane and its copolymers, silicone and its copolymers, ethylene vinyl-acetate, thermoplastic elastomers, polyvinyl chloride, polyolefins, cellulose, polyamides, polyesters, polysulfones, polytetrafluoroethylenes, polycarbonates, acrylonitrile butadiene styrene copolymers, acrylics, polylactic acid, polyglycolic acid, polycaprolactone, polylactic acid-polyethylene oxide copolymers, cellulose, collagens, and chitins.

66. A method according to claim 61, wherein the device provides a surface selected from the group consisting of titanium/titanium alloys, TiNi, aluminum oxide, platinum/platinum alloys, stainless steels, pyrolytic carbon, silver, glassy carbon, polyurethanes, polycarbonates, silicone elastomers, polyolefins, polyvinyl chlorides, polyethers, polyesters, nylons, polyvinyl pyrrolidones, polyacrylates polymethacrylates, n-butyl cyanoacrylate, polyvinyl alcohols, polyisoprenes, rubber, cellulotics, polyvinylidene fluoride, polytetrafluoroethylene, ethylene tetrafluoroethylene copolymer, acrylonitrile butadiene ethylene, polyamide, polyimide, styrene acrylonitrile, hydroxyapatite, bone, skin, teeth, collagen, laminin, elastin, fibrin, wood, cellulose, compressed carbon and glass.

67. A composition according to claim 1 wherein the polyether monomer comprises an alkoxy (poly)alkyleneglycol (meth)acrylate, the carboxylic acid-containing monomer is selected from carboxyl substituted ethylene compounds, the photoderivatized monomer is selected from the group consisting of N-[3-(4-benzoylbenzoamido)propyl]methacrylamide, 9-vinyl anthracene, and 9-anthracenylmethyl methacrylate, and the hydrophilic monomer is selected from the group consisting of acrylamide, N-vinylpyrrolidone, methacrylamide, and acrylamido propanesulfonic acid (AMPS).

68. A composition according to claim 67 wherein the medicament is selected from the group consisting of gene therapy agents selected from therapeutic nucleic acids and nucleic acids encoding therapeutic gene products, antibiotics selected from penicillin, tetracycline, chloramphenicol, minocycline, doxycycline, vancomycin, bacitracin, kanamycin, neomycin, gentamycin, erythromycin and cephalosporins and antiseptics selected from silver sulfadiazine, chlorhexidine, glutaraldehyde, peracetic acid, sodium hypochlorite, phenols, phenolic compounds, iodophor compounds, quaternary ammonium compounds, and chlorine compounds

and the device is selected from the group consisting of catheters, implantable vascular access ports, blood storage bags, vascular stents, blood tubing, central venous catheters, arterial catheters, vascular grafts, intraaortic balloon pumps, heart valves, cardiovascular sutures, total artificial hearts and ventricular assist pumps, extracorporeal devices such as blood oxygenators, blood filters, hemodialysis units, hemoperfusion units, plasmapheresis units, hybrid artificial organs such as pancreas or liver and artificial lungs and filters adapted for deployment in a blood vessel in order to trap emboli.

69. A composition according to claim 67, wherein the device provides a polymeric surface selected from the group consisting of polyurethane and its copolymers, silicone and its copolymers, ethylene vinyl-acetate, thermoplastic elastomers, polyvinyl chloride, polyolefins, cellulotics, polyamides, polyesters, polysulfones, polytetrafluoroethylenes, polycarbonates, acrylonitrile butadiene styrene copolymers, acrylics, polylactic acid, polyglycolic acid, polycaprolactone, polylactic acid-polyethylene oxide copolymers, cellulose, collagens, and chitins.

70. A composition according to claim 67, wherein the device provides a surface selected from the group consisting of titanium/titanium alloys, TiNi, aluminum oxide, platinum/platinum alloys, stainless steels, pyrolytic carbon, silver, glassy carbon, polyurethanes, polycarbonates, silicone elastomers, polyolefins, polyvinyl chlorides, polyethers, polyesters, nylons, polyvinyl pyrrolidones, polyacrylates polymethacrylates, n-butyl cyanoacrylate, polyvinyl alcohols, polyisoprenes, rubber, cellulotics, polyvinylidene fluoride, polytetrafluoroethylene, ethylene tetrafluoroethylene copolymer, acrylonitrile butadiene ethylene, polyamide, polyimide, styrene acrylonitrile, hydroxyapatite, bone, skin, teeth, collagen, laminin, elastin, fibrin, wood, cellulose, compressed carbon and glass.

71. A crosslinked composition according to claim 21 wherein the polyether monomer comprises an alkoxy (poly)alkyleneglycol (meth)acrylate, the carboxylic acid-containing monomer is selected from carboxyl substituted ethylene compounds, the photoderivatized monomer is selected from the group consisting of N-[3-(4-

5 benzoylbenzoamido)propyl]methacrylamide, 9-vinyl anthracene, and 9-anthracenylmethyl methacrylate, and the hydrophilic monomer is selected from the group consisting of acrylamide, N-vinylpyrrolidone, methacrylamide, and acrylamido propanesulfonic acid (AMPS).

72. A crosslinked composition according to claim 71 wherein the medicament is selected from the group consisting of gene therapy agents selected from therapeutic nucleic acids and nucleic acids encoding therapeutic gene products, antibiotics selected from penicillin, tetracycline, chloramphenicol, minocycline, doxycycline, vancomycin, bacitracin, kanamycin, neomycin, gentamycin, erythromycin and cephalosporins and antiseptics selected from silver sulfadiazine, chlorhexidine, glutaraldehyde, peracetic acid, sodium hypochlorite, phenols, phenolic compounds, iodophor compounds, quaternary ammonium compounds, and chlorine
15 compounds and the device is selected from the group consisting of catheters, implantable vascular access ports, blood storage bags, vascular stents, blood tubing, central venous catheters, arterial catheters, vascular grafts, intraaortic balloon pumps, heart valves, cardiovascular sutures, total artificial hearts and ventricular assist pumps, extracorporeal devices such as blood oxygenators, blood filters, hemodialysis units, hemoperfusion units, plasmapheresis units, hybrid
20 artificial organs such as pancreas or liver and artificial lungs and filters adapted for deployment in a blood vessel in order to trap emboli.

73. A crosslinked composition according to claim 71, wherein the device provides a polymeric surface selected from the group consisting of polyurethane and its copolymers,

silicone and its copolymers, ethylene vinyl-acetate, thermoplastic elastomers, polyvinyl chloride, polyolefins, cellulotics, polyamides, polyesters, polysulfones, polytetrafluoroethylenes, polycarbonates, acrylonitrile butadiene styrene copolymers, acrylics, polylactic acid, polyglycolic acid, polycaprolactone, polylactic acid-polyethylene oxide copolymers, cellulose, collagens, and chitins.

74. A crosslinked composition according to claim 71, wherein the device provides a surface selected from the group consisting of titanium/titanium alloys, TiNi, aluminum oxide, platinum/platinum alloys, stainless steels, pyrolytic carbon, silver, glassy carbon, polyurethanes, polycarbonates, silicone elastomers, polyolefins, polyvinyl chlorides, polyethers, polyesters, nylons, polyvinyl pyrrolidones, polyacrylates polymethacrylates, n-butyl cyanoacrylate, polyvinyl alcohols, polyisoprenes, rubber, cellulotics, polyvinylidene fluoride, polytetrafluoroethylene, ethylene tetrafluoroethylene copolymer, acrylonitrile butadiene ethylene, polyamide, polyimide, styrene acrylonitrile, hydroxyapatite, bone, skin, teeth, collagen, laminin, elastin, fibrin, wood, cellulose, compressed carbon and glass.

75. A method according to claim 41 wherein the polyether monomer comprises an alkoxy (poly)alkyleneglycol (meth)acrylate, the carboxylic acid-containing monomer is selected from carboxyl substituted ethylene compounds, the photoderivatized monomer is selected from the group consisting of N-[3-(4-benzoylbenzoamido)propyl]methacrylamide, 9-vinyl anthracene, and 9-anthracenylmethyl methacrylate, and the hydrophilic monomer is selected from the group consisting of acrylamide, N-vinylpyrrolidone, methacrylamide, and acrylamido propanesulfonic acid (AMPS).

76. A method according to claim 75 wherein the medicament is selected from the group consisting of gene therapy agents selected from therapeutic nucleic acids and nucleic acids

encoding therapeutic gene products, antibiotics selected from penicillin, tetracycline, chloramphenicol, minocycline, doxycycline, vancomycin, bacitracin, kanamycin, neomycin, gentamycin, erythromycin and cephalosporins and antiseptics selected from silver sulfadiazine, chlorhexidine, glutaraldehyde, peracetic acid, sodium hypochlorite, phenols, phenolic compounds, iodophor compounds, quaternary ammonium compounds, and chlorine compounds and the device is selected from the group consisting of catheters, implantable vascular access ports, blood storage bags, vascular stents, blood tubing, central venous catheters, arterial catheters, vascular grafts, intraaortic balloon pumps, heart valves, cardiovascular sutures, total artificial hearts and ventricular assist pumps, extracorporeal devices such as blood oxygenators, blood filters, hemodialysis units, hemoperfusion units, plasmapheresis units, hybrid artificial organs such as pancreas or liver and artificial lungs and filters adapted for deployment in a blood vessel in order to trap emboli.

77. A method according to claim 75, wherein the device provides a polymeric surface selected from the group consisting of polyurethane and its copolymers, silicone and its copolymers, ethylene vinyl-acetate, thermoplastic elastomers, polyvinyl chloride, polyolefins, cellulose, polyamides, polyesters, polysulfones, polytetrafluoroethylenes, polycarbonates, acrylonitrile butadiene styrene copolymers, acrylics, polylactic acid, polyglycolic acid, polycaprolactone, polylactic acid-polyethylene oxide copolymers, cellulose, collagens, and chitins.

78. A method according to claim 75, wherein the device provides a surface selected from the group consisting of titanium/titanium alloys, TiNi, aluminum oxide, platinum/platinum alloys, stainless steels, pyrolytic carbon, silver, glassy carbon, polyurethanes, polycarbonates, silicone elastomers, polyolefins, polyvinyl chlorides, polyethers, polyesters, nylons, polyvinyl

pyrrolidones, polyacrylates polymethacrylates, n-butyl cyanoacrylate, polyvinyl alcohols,
polyisoprenes, rubber, cellulosics, polyvinylidene fluoride, polytetrafluoroethylene, ethylene
tetrafluoroethylene copolymer, acrylonitrile butadiene ethylene, polyamide, polyimide, styrene
acrylonitrile, hydroxyapatite, bone, skin, teeth, collagen, laminin, elastin, fibrin, wood, cellulose,
5 compressed carbon and glass.

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